

LIDEXANEXETAMINE DIMESTYLATE (VYVANSE™) ANALYTICAL PROFILE

ANALYTICAL PROFILE OF LIDEXANEXETAMINE DIMESTYLATE (VYVANSE™)

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Submitted: 12 March 2008
Accepted: 9 April 2008

INTRODUCTION

Vyvanse™ (lisdexamfetamine dimesylate) is a drug in a new class of long-acting prodrug stimulants for Attention-Deficit/Hyperactivity Disorder (ADHD) (Fig. 1). Vyvanse™ was approved by the FDA in February 2007 and is a Federal Schedule II controlled substance. Vyvanse™ is manufactured by New River Pharmaceuticals, Inc. and distributed by Shire, Inc.

Lisdexamfetamine (aka "Lidex" or "LDX") is unique from other ADHD drugs because it is a prodrug of *d*-amphetamine designed in part to reduce the potential for abuse. A prodrug is a pharmaceutical substance which is therapeutically inactive until metabolized in the body. In the case of Vyvanse™, *d*-amphetamine is covalently linked to the amino acid *D*-lysine (Fig. 2). Once lisdexamfetamine passes through the gastrointestinal tract and liver, it is converted to active *d*-amphetamine [1].

Vyvanse™ is currently supplied in three dosage strengths with the following capsule colors and logo markings:

Dosage	Capsule Colors	Imprint
30 mg	white/orange	NRP103 30 mg
50 mg	white/blue	NRP104 50 mg
70 mg	blue/orange	NRP104 70 mg

During the second quarter of 2008, three more dosage strengths (20, 40 and 60 mg) will become available for use [2].

Examination of Reference Standard Dose

Reference standard: A 760 mg (twelve) reference powder was obtained from Shire, Inc., and ten 30 mg capsules were purchased from a local pharmacy.

GC-MS analysis: A portion of the reference powder was dissolved in methanol. Analysis was performed on a HP 6890/5973 GC-MS (EI) with a HP-5 ms column using a ramped general temperature program.

FTIR analysis: FTIR analysis was performed using a Perkin Elmer Spectrum 100 with a single beam diamond ATR.

Alkaline hydrolysis procedure: One capsule was tested with alkaline hydrolysis to determine if amphetamine could be produced *in vivo*. The contents were made basic with saturated NaOH and heated in a 70° C water bath for approximately 30 minutes. The sample was then extracted with CHCl₃ and analyzed by GC-MS.



Fig. 1 Lisdexamfetamine dimesylate; MW~ 455.60

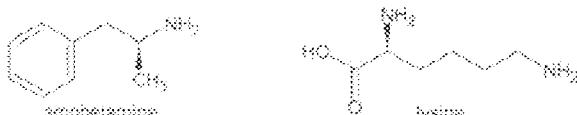


Fig. 2 Amphetamine and lysine structures

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Chemical Characterization of Vyvanse® (Lisdexamfetamine Dimesylate) Powder

Results and Discussion

Four color tests were performed on both the epoxide and reference powder with the following results:

Reagent	Color Change
Magnes.	orange to brown
Liebermann's	orange
sodium nitroprusside	no color change
acidified rotsch thioacetone	no color change

The mass spectrum (Fig. 2) of the methanol extract for lisdexamfetamine produced a base ion at m/z 83 with a molecular ion at m/z 163. Other major ions present include m/z 161, 91, 173, and 155.

FTIR-ATR data (Fig. 4) produced principle absorption bands at 1634, 1543, 1613, 1187, and 1016 cm⁻¹.

The alkaline hydrolysis of lisdexamfetamine produced a trace of amphetamine (Figs. 3 and 5).

Conclusion

Analytical data consisting of color tests, GC-MS and FTIR-ATR was presented to aid the analysis with the identification and confirmation of lisdexamfetamine. The alkaline hydrolysis procedure has shown that amphetamine can be cleaved from the lysine group although an appreciable amount was not produced under the stated conditions.

Acknowledgments

1. Sandra Williams, Shire, Inc. for providing the standard
2. Agent Tim McKibbon, CSH, for sharing his data

References

1. Vyvanse™ "Medication Guide", Shire Pharma sciculus Inc., retrieved from <http://www.vyvanse.com> on September 11, 2007.
2. Press release announcement reviewed from <http://www.shireadmelements.com> on March 3, 2008.

ESI-MS/MS Spectrum (positive ion mode) of Idoxamidium dimers

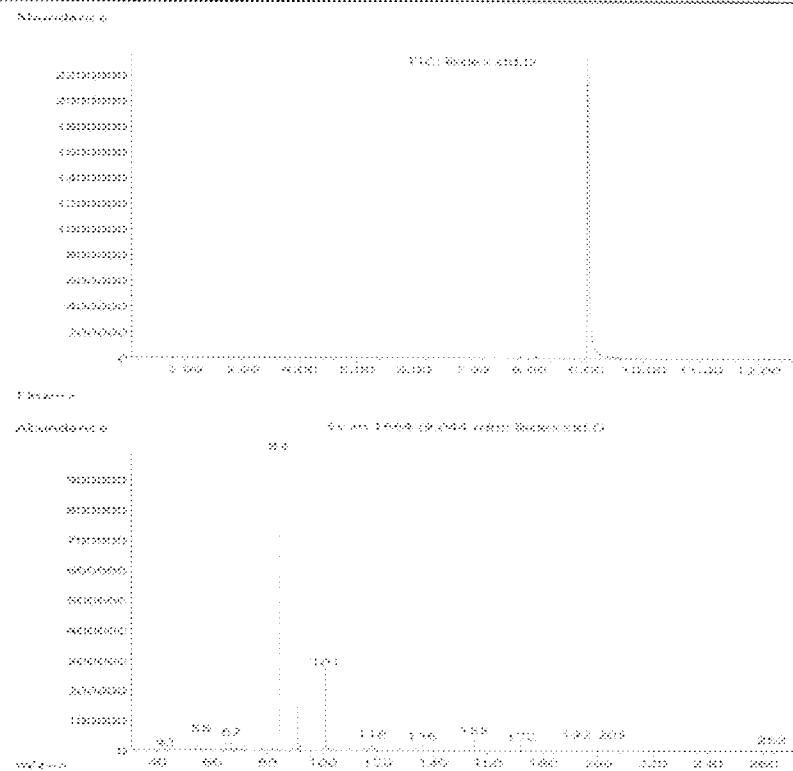


Fig. 3 ESI and mass spectrum of Idoxamidium; MW = 263.14

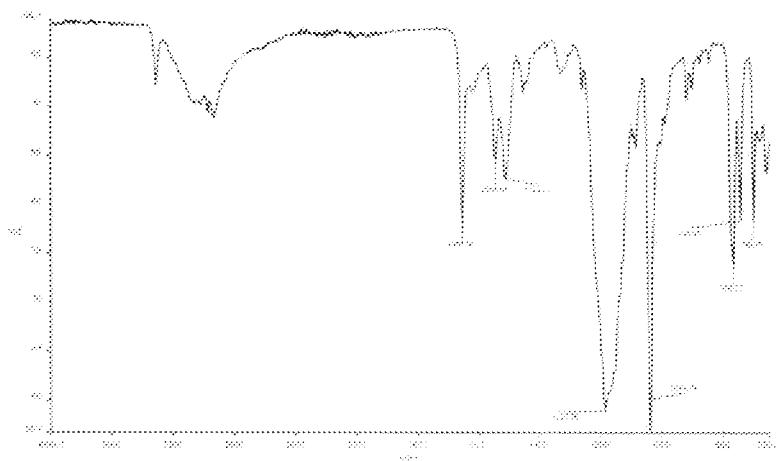


Fig. 4 FTIR-ATR of Idoxamidium dimer

Chromatogram Obtained from Alkaline Hydrolysis of Hexadraconamine

